

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of:

NAKAI *et al.*

Art Unit: 1633

Application No.: 09/897,988

Examiner: Maria Marvich

Filing Date: July 5, 2001

Attorney Ref. No.: US-142O

For: METHOD FOR PRODUCING SUBSTANCE  
UTILIZING MICROORGANISM

Confirmation No.: 1677

**REPLY BRIEF FOR APPELLANT**

**Mail Stop Appeal Brief - Patents**

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

COMES NOW the Appellant to present this Reply Brief in support of the appeal of the final rejection of Claims 1, 6 and 12-17 contained in the Office Action dated June 11, 2010 (“Final Rejection”), and to respond to the Examiner’s Answer dated April 4, 2011 in the above-captioned patent application. A petition for an extension of time is not necessary, as this Reply Brief is being filed within two months of the mailing of the Examiner’s Answer.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. If, however, additional extensions of time are necessary to prevent abandonment of this application or dismissal of this appeal, then such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is hereby authorized to charge fees necessitated by this paper, and to credit all refunds and overpayments, to deposit account 50-2821.

For the following reasons, Appellant respectfully submits that the final rejection of each of Claims 1, 6, and 12-17 in this application is in error, and therefore respectfully requests reversal of the rejections.

**I. Status of Claims**

Claims 1, 6 and 12-17 are pending. Claims 1, 6 and 12-17 stand finally rejected in the Final Office Action of June 11, 2010.

**II. Grounds of Rejections to Be Reviewed on Appeal**

The Office Action includes a single (compound) rejection to be reviewed on appeal, the rejection of Claims 1, 6, and 12-17 under 35 U.S.C. § 103(a) as reciting subject matters that allegedly would have been obvious, and therefore allegedly are unpatentable, over U.S. Patent No. 5,830,716, granted to Kojima *et al*, in view of Calhoun *et al* (*J. Bacteriol.* 1993 May; 175(10), pp. 3020-3025), or Ciccognani *et al* (*FEMS Microbiology Letters* 94, 1992, pp. 1-6), or Kusumoto *et al* (*Arch. Microbiol.*, 200, Vol. 173, pp 390-397), or Sone *et al* (Collection of Summaries of Lectures made at the Meeting of Japan Bioengineering Association, Sept. 15, 1995, p. 10).

### III. Argument

This reply brief is filed to specifically address select statements made in the Examiner's Answer dated April 4, 2011.

Specifically, on page 13 of the Examiner's Answer, it is stated

"[i]n no [sic] way, can Eggeling et al. be taken to argue that any global reduction in growth will lead to improve amino acid production. It is inherent in the alterations [sic] produced by Eggeling et al that the growth yield is concomitant with increased lysine and that is through [sic] reduced threonine. The cell is responsive to the decreased flux towards threonine by reducing growth yield and lysine production."

However, although Eggeling discloses only one example of lysine production using dapA, Eggeling concludes from this example that the concept of growth limitation is generalized to general metabolite production as follows: "[t]his does not only achieve an increase in lysine yield, but this example of an intracellularly introduced growth limitation is proposed as a new general means of increasing flux for industrial metabolite overproduction" (see Abstract of Eggeling), and "[t]herefore, similar growth limitations, introduced by recombinant DNA techniques, are proposed as an attractive means for the improvement of further metabolite production processes" (see page 30 of Eggeling).

As for Hollander et al., the Examiner's Answer states on page 13:

"[i]n the case of Hollander et al the limitation on biomass is a consequence of limiting carbon and/or phosphorous which step is not utilized in the instant rejection. Rather, the genetic alterations of the instant claims are designed to modulate the cell for improved growth yield and improved amino acid production wherein phosphorous and carbon are not limited."

However, Hollander was not presented to show the present invention or try to replicate the instant rejection, and so the statement above "which is not utilized in the instant rejection" is irrelevant and non-applicable. This document was presented to demonstrate the importance of limiting bacterial growth in amino acid production and also to show the state of the art at the time of filing of the invention. It should be noted that carbon and phosphorous limitation are only used in this method to limit growth.

As shown in these documents, it was a common knowledge at the time of filing of the present application that limiting growth yield is important for amino acid production so as to decrease the carbon flow to cell synthesis and increase the carbon flow to amino acid

biosynthesis. These documents clearly show this fact, which is important for understanding the non-obviousness of the claimed invention. Eggeling achieved growth inhibition by modifying the bacteria (breeding), and Hollander achieved the same by modifying the fermentation process (nutrients). The concept of growth inhibition is applicable to general amino acid production regardless of the specific genetic modifications or the specific culture conditions.

Eggeling and Hollander clearly would provide a negative motivation to the person of ordinary skill in the art to make the claimed modification to enhance cytochrome bo-type oxidase activity because of the teaching that such a modification might lead to increased yield of the bacterium and decreased amino acid production. Therefore, the effect of the present invention would have never been expected by the person of ordinary skill in the art and the claimed invention is not obvious over the cited references.

Finally, on page 14, the Examiner wonders how the interpretation that the references are “analyzed in independently in combination with Kojima [*sic*]” has prevailed. This interpretation is clear from the statement of the rejection throughout prosecution, and is stated again in the Examiner’s Answer. Specifically, the statement of rejection is ‘Kojima in view of Calhoun, Ciccognani, **or** Kusomoto **or** Sone.’ In the English language, the word “or” is a conjunction that unequivocally indicates that the elements are to be conjoined in the alternative. The statement of the rejection, with the secondary references recited as shown above, was repeatedly made during prosecution, and is also present as recited above on page 5 of the Examiner’s Answer. Even when there is not a conjunction between each and every element in a string of elements, the word “or” means that each element is present in the alternative, so the lack of a conjunction between Calhoun and Ciccognani does not indicate that they can be viewed in any way other than in the alternative. It is the only way this statement of rejection **can be interpreted**. Furthermore, nothing in the prosecution implied a different interpretation. Finally, there is nothing to ‘interpret’. The secondary references are cited in the alternative in the statement of the rejection. The Examiner cannot claim that they are NOT to be taken in the alternative, since this is directly contradictory to the plain meaning of the statement of rejection. The rejection must stand or fall as recited.

**IV. Conclusion**

For at least the foregoing reasons, Appellant respectfully submits that the subject matters of Claims 1, 6, and 12-17, each taken as a whole, are patentable. Accordingly, Appellant respectfully requests reversal of the rejections of Claims 1, 6, and 12-17 under section 103(a).

Respectfully submitted,

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